



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,469	10/31/2001	Aya Jakobovits	511582002420	3304

36327 7590 06/16/2004

AGENSYS C/O MORRISON & FOERSTER LLP
3811 VALLEY CENTRE DRIVE, SUITE 500
SAN DIEGO, CA 92130

EXAMINER

DAVIS, MINH TAM B

ART UNIT PAPER NUMBER

1642

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/001,469

Applicant(s)

JAKOBOVITS ET AL.

Examiner

MINH-TAM DAVIS

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07/28/04.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48, 50 and 53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48, 50 and 53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>04/13/04</u> ; <u>04 109102</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's election with traverse of group XIV which would be rejoined with group XV, as per interview of 25 June 2002, Claims 48, 50, 53 in Paper of 07/28/03 is acknowledged and entered.

Claims 48, 50, 53 are pending in the instant application. It is noted that the claims submitted on 02/23/04 are the original claims that are included with the substituted specification.

Groups XIV-XV, Claims 48, 50, 53, are currently under prosecution, since group XIV has been rejoined with group XV.

The traversal is on the following ground(s):

Applicant asserts that on 25 June 2003, the Office would recombine several of the currently pending Groups as encompassing subject matter that is not separately restrictable, without further action on the part of the Applicants. These Groups include the recombination of Groups II and III, the recombination of Groups V and VI, the recombination of Groups VIII and IX, the recombination of Groups XII and XIII, the recombination of Groups XIV and XV, and the recombinations of Groups XVI and XVII.

Applicants traverse on the following grounds:

(1) The manner/modality in which the function, production or status of 101P3A1 1 protein is evaluated is not dispositive of the invention as set forth in the specification and claims. Of particular importance, independent claim 48 is not limited as to the modality by which expression status is observed nor a particular expression status parameter;

Art Unit: 1642

(2) The fact that four claims are broken into 19 (or 13) groups is inconsistent with Applicants' right to define their invention, the invention is instead being defined by the Office with omission of desired subject matter;

(3) The subject matter of dependent claims 51-52 (presently cancelled) is not separately restrictable and, at most, a species election might be appropriate in light of generic/linking claim 48; and

(4) No undue search burden is present.

The Examiner acknowledges that as per discussion of the interview of 25 June 2003, the following groups have been recombined: The recombination of Groups II and III, the recombination of Groups V and VI, the recombination of Groups VIII and IX, the recombination of Groups XII and XIII, the recombination of Groups XIV and XV, and the recombinations of Groups XVI and XVII.

The arguments have been considered but are found not to be persuasive for the following reasons:

1) The independent claim 48 is a linking claim, which links different groups, I, (II-III), IV, (V-VI), VII, (VIII-IX), X, XI, (XII-XIII), (XIV-XV), (XVI-XVII), XVIII, XIX, which are distinct because they have different methods steps, reagents and/or dosages, and/or schedules used, response variables and criteria for success, as set forth in the previous Office action.

As a linking claim, claim 48 was not limited by the Examiner as to the modality by which expression status is observed nor a particular expression status parameter.

Art Unit: 1642

Further, as dependent on the linking claim, claim 48, different groups are not species at the time of examination, which is subject to the nonallowance of the linking claim (see MPEP 804.01).

In addition, the invention is not defined by the Office. Different groups are restricted based on the disclosure in the specification and in the claims, especially the now abandoned claims 51-52.

Moreover, the searches for different groups are not co-extensive, and it would be a serious burden for the Examiner to search all the groups together.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, groups XIV-XV, claims 48, 50, 53 are examined in the instant application.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER

Claims 48, 50, 53 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

The limitation of a method for identifying an agent that decreases the expression status of 101P3A11 comprising observing “at least” one “property characteristic of the expression status” of 101P3A11 in claim 48 has no clear support in the specification and the claims as originally filed.

A review of the specification finds support for parameters that can be used for evaluate the status of 101P3A11, and for alteration in the status of 101P3A11 which comprises a change in the location of 101P3A11 and/or 101P3 A11 expressing cells

Art Unit: 1642

and/or an increase in 101P3A11 mRNA and/or protein expression (p.37-39, under item VIII). Although the specification discloses parameters that can be used for evaluating status of 101P3A11, and alteration in the status of 101P3A11, there is no disclosure of "property characteristic of the expression status" nor "at least" one of said property.

The subject matter claimed in claims 48, 50, 53 broadens the scope of the invention as originally disclosed in the specification.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Claims 48, 50, 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 48, 50, 53 are indefinite because it is not clear what constitutes "expression status" recited in claims 48, 53.

The specification discloses that "status" refers to the "condition" or "state" of a gene and its products (p.37, paragraph before last). The specification discloses that "typically", one uses a number of parameters to evaluate the condition or state of a gene, and its products, these parameters "include, but not limited to" the location of the expressed gene production, including the location of 101P3A11 expressing cells, as well as the level, and biological activity of expressed gene products (such as 101P3A11 mRNA, polynucleotides and polypeptides). The specification further discloses that "typically", an alteration in the status of 101P3A11 comprises a change in the location of 101P3A11 and/or 101P3A11 expressing cells and/or an increase in 101P3A11 mRNA and/or protein expression.

It is noted that there is no definition of "expression status" and thus one would not know what constitutes "expression status" and therefore, one would not know what constitutes "a decrease in the expression status" in the claimed invention.

The term "expression status" in claims 48, 53 is a relative term which renders the claim indefinite. The term "expression status" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the expression status as claimed the invention.

A claim is indefinite where those skilled in the art would not understand what is claimed, when reading the claim language in light of the specification and prosecution history. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1218, 18 USPQ2d 1016, 1030 (Fed. Cir. 1991); *Texas Instruments Inc. v. United States Int'l Trade Commission*, 871 F.2d 1054, 1063, 10 USPQ2d 1257, 1263-64 (Fed. Cir. 1989); *Orthokinetics, Inc.*, 806 F.2d at 1576, 1 USPQ2d at 1088.

2. Claims 48, 50, 53 are indefinite because it is not clear what constitutes "at least a property characteristic of the expression status" recited in claim 48, since there is no definition of the property characteristic of the expression status. Further, since it is not clear what constitutes "expression status", it is not clear what constitutes the "properties characteristics of the expression status".

3. Claim 53 is indefinite for the use of the language "association". It is not clear what type of association is referred to.

Art Unit: 1642

4. Claim 53 is indefinite for the use of the language “other proteins”. It is not clear what are “other proteins” that are referred to.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 1-5, 8-11, 16, 19-20 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 48, 50 are drawn to a method for identifying an agent that decreases the expression status of 101P3A11 protein, comprising determining a diminution in at least “one property characteristic of the expression status” of “101P3A11 protein” in the presence of said agent.

Claim 53 is drawn to a method for identifying an agent that decreases the expression status of 101P3A11 protein, comprising determining a diminution in the association of 101P3A11 with “other proteins” in the presence of said agent.

The specification, figure 3 legend on page 6 discloses amino acid sequence of 101P3A11 (SEQ ID NO:2866).

The specification discloses that “status” refers to the “condition” or “state” of a gene and its products (p.37-39, under item VIII). The specification discloses that “typically”, one uses a number of parameters to evaluate the condition or state of a

Art Unit: 1642

gene, and its products, these parameters “include, but not limited to” the location of the expressed gene production, including the location of 101P3A11 expressing cells, as well as the level, and biological activity of expressed gene products (such as 101P3A11 mRNA, polynucleotides and polypeptides). The specification further discloses that “typically”, an alteration in the status of 101P3A11 comprises a change in the location of 101P3A11 and/or 101P3A11 expressing cells and/or an increase in 101P3A11 mRNA and/or protein expression (p.37, paragraph before last).

It is noted that since there is no definition of expression status in the specification, one does not know what constitutes “expression status” of 101P3A11. Further, although the specification discloses parameters that can be used for evaluating status of 101P3A11, and although the specification discloses alteration of the status of 101P3A11, however, since there is no definition of expression status and since one does not know what constitutes “expression status” of 101P3A11, one does not know what constitutes “a property characteristic of the expression status of 101P3A11”.

In addition, it is further noted that “other proteins” encompass any proteins of diverse structure, that are “associated” with 101P3A11 protein, wherein association encompasses any type of association. There is no disclosure in the specification of the common structure of “other proteins” that are “associated” with 101P3A11 protein.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University

of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that [a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials. Id. At 1567, 43 USPQ2d at 1405. The court also stated that

a generic statement such as vertebrate insulin cDNA or mammalian insulin cDNA without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling

within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristicsi.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of a property characteristic of the expression status of 101P3A11 or other proteins, per Lilly by structurally describing a representative number of a property characteristic of the expression status of 101P3A11, or other proteins by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus. Alternatively, per Enzo, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying

Art Unit: 1642

characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.”

In this case, the specification does not describe a property characteristic of the expression status of 101P3A11, or other proteins to practice the method of claims 48, 50, 53 in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any property characteristic of the expression status of 101P3A11, any other proteins associated with 101P3A11, nor does the specification provide any partial structure of such other proteins, nor any physical or chemical characteristics of other proteins, other than SEQ ID NO:2866, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single protein of SEQ ID NO:2866, this does not provide a description of a property characteristic of the expression status of 101P3A11, or other proteins that would satisfy the standard set out in Enzo.

The specification also fails to describe a property characteristic of the expression status of 101P3A11, or other proteins by the test set out in Lilly. The specification describes only a single protein of SEQ ID NO:2866. Therefore, it necessarily fails to describe a “representative number” of such species. In addition, the specification also does not describe “structural features common to the members of the genus, which features constitute a substantial portion of the genus.”

Thus, the specification does not provide an adequate written description of a property characteristic of the expression status of 101P3A11, or other proteins that is required to practice the claimed invention. Since the specification fails to adequately describe the product, it also fails to adequately describe the method using said product.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Claims 48, 50, 53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 48, 50 are drawn to a method for identifying an agent that decreases the expression status of "101P3A11 protein", comprising determining a diminution in at least one property characteristic of the expression status of "101P3A11 protein" in the presence of said agent.

Claim 53 is drawn to a method for identifying an agent that decreases the expression status of "101P3A11 protein", comprising determining a diminution in the association of 101P3A11 with "other proteins" in the presence of said agent.

A. Claims 48, 50, 53 are rejected under 112, first paragraph, because **one would not know how to use the claimed method, in view that one does not know what constitutes "expression status" nor "at least one property characteristic of the**

Art Unit: 1642

expression status of 101P3A11 protein”, and thus one does not know how to determine the diminution of said property.

The specification discloses that “status” refers to the “condition” or “state” of a gene and its products, and methods for monitoring the status of 101P3A11 (p.37-39, under item VIII). The specification discloses that “typically”, one uses a number of parameters to evaluate the condition or state of a gene, and its products, these parameters “include, but not limited to” the location of the expressed gene production, including the location of 101P3A11 expressing cells, as well as the level, and biological activity of expressed gene products (such as 101P3A11 mRNA, polynucleotides and polypeptides) (p.37). The specification further discloses that “typically”, an alteration in the status of 101P3A11 comprises a change in the location of 101P3A11 and/or 101P3A11 expressing cells and/or an increase in 101P3A11 mRNA and/or protein expression (p.37, paragraph before last). The specification discloses that the expression status of 101P3A11 “provides” information including the presence, stage and location of dysplastic, precancerous and cancerous cells (p.38, third paragraph).

It is noted that since there is no definition of “expression status” or condition or state of a gene or its product, and thus one would not know what constitutes “expression status” and what constitutes a decrease or an alteration in the expression status in the claimed invention.

Further, since there is no definition of “the property characteristic of the expression status”, and since it is not clear what constitutes “expression status”, it is not clear what constitutes the “properties characteristics of the expression status”.

Art Unit: 1642

Further, since the definition of an alteration of the status of 101P3A11 in the specification, on page 37, paragraph before last, is not limiting, an alteration in the status of 101P3A11 would comprise “any type of changes” related to 101P3A11, and is not limited to a change in the location of 101P3A11 and/or 101P3A11 expressing cells and/or an increase in 101P3A11 mRNA and/or protein expression (p.37, paragraph before last); for example, any mutation including naturally occurring mutation, at any position of SEQ ID NO:2866 , which the specification has not taught how to make (see rejection under variants below) .

Thus although the specification discloses methods for monitoring the status of 101P3A11, and although the specification discloses an alteration in the status of 101P3A1, one would not know how to use the claimed method, in view that one does not know what constitutes “expression status” nor “at least one property characteristic of the expression status of 101P3A11 protein”, and thus one does not know how to determine the diminution of said property. Further, one would not know how to make or identify the numerous alterations of the status of 101P3A11, for use in the claimed method.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

Art Unit: 1642

B. Further, claim 53 is rejected under 112, first paragraph, because one would not know how to use the claimed method, in view that one cannot determine what other proteins are associated with 101P3A11.

Since there is no definition of “association” with 101P3A11 and “other proteins”, “other proteins” encompass any protein of any structure.

Applicant does not disclosed how to make such “other proteins” for use in the claimed method.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

C. Claims 48, 50, 53 are rejected under 112, first paragraph, because claims 48, 50, 53 encompass a method for identifying an agent that decreases the expression status of “variants” of the 101P3A11 protein of SEQ ID NO:2866.

Claims 48, 50, 53 as written encompass a method for identifying an agent that decreases the expression status of “a variant of the wild type101P3A11 protein of SEQ ID NO:2866”, comprising determining: 1) a diminution in at least one property characteristic of the expression status of a variant of SEQ ID NO:2866, or 2) a diminution in the association of a variant of SEQ ID NO:2866 with “other proteins” in the presence of said agent, because 101P3A1 encompasses wild type and variant 101P3A11.

Applicants have not shown how to make and use the claimed variants which are capable of functioning or have the properties of SEQ ID NO:2866.

The claims read on variants of SEQ ID NO:2866, wherein said variants have any type of substitution besides conservative substitution, at any amino acid, throughout the length of the peptide, as well as insertions and deletions. The specification and the claims do not place any limit on which amino acid to be subjected to conservative or non-conservative substitution, the type of substitution besides conservative substitution, nor the type of amino acids replacing the original amino acids. In addition, the specification do not place any limit on the number of amino acids that could be substituted. Thus the scope of the claims includes nucleotide sequences encoding numerous structural variants. The specification and the claims do not provide any guidance as to which, or how many original amino acid(s) to be substituted, or to which type of substitution besides conservative substitution, or which amino acids could be deleted or inserted so that the claimed polypeptide could function as contemplated. No consensus sequence for the claimed polypeptide is disclosed in the specification.

One cannot extrapolate the teaching in the specification to the scope of the claims because one cannot predict that the polypeptide sequences used in the claimed method would have properties related to that of SEQ ID NO:2866. It is well known in the art that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. For example, Bowie et al (Science, 1990, 257 : 1306-1310) teach that an amino acid sequence encodes a message that determine the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instruction of the

Art Unit: 1642

genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (col.1, p.1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitution can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col.2, p.1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al, (Journal of Cell Biology, 1990, 11: 2129-2138), who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. The Journal of Immunology, 1989, 143(8): 2595-2601, and Gillies et al. Human Antibodies and Hybridomas, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential

Art Unit: 1642

chemical modification will often dramatically affect the biological activity and characteristic of a protein.

Since Applicant has not shown how to make variants of SEQ ID NO:2866, such that they would function as claimed, one would not know how to use said variants in the claimed method for determining agents that decreases the expression status of said variants.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, CHRISTINA CHAN can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1642

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

June 05, 2004

SUSAN WINGAR, PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Susan', followed by a large, stylized flourish or initial.